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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,168	02/07/2001	David J. Wright	P-4423D1	8991

26253 7590 08/23/2004

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EXAMINER	
FORMAN, BETTY J	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 08/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/778,168	WRIGHT ET AL.	
	Examiner	Art Unit	
	BJ Forman	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. This action is in response to papers filed 25 March 2004 in which the previous rejection was traversed.

The previous rejections in the Office Action dated 8 July 2003 are withdrawn in view of Applicant's remarks and new grounds for rejection. Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the withdrawn rejections and new grounds for rejection discussed below.

Claims 1 and 3-22 are under prosecution.

Claim Objections

2. Claim 20 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of Claim 19. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 20 is further objected to because the claim is identified as "original". However, original Claim 20 is reproduced below:

"The method of Claim 19 wherein a change in fluorescence polarization is detected as an indication of the presence of the single nucleotide polymorphism."

Hence, Claim is incorrectly identified and inappropriately amended.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1 and 2-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 2-22 are indefinite in Claim 1 because the preamble recites "in an isothermal target amplification reaction" however the method does not recite steps of isothermal amplification. Therefore, it is unclear whether isothermal amplification is required by the method.

Claims 7-12 are indefinite in Claim 7 for the recitation "the nondiagnostic nucleotide" because the recitation lacks proper antecedent basis in Claim 1.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1, 3-5, 7-8, 11-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996).

Regarding Claim 1, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. $\beta+$ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54). While the method steps do not require isothermal amplification, Caskey et al teach the amplification via hybridization and primer extension (as claimed) wherein the extension utilizes DNA polymerase (Klenow) at a single temperature e.g. 37° C for 30 minutes (Column 8, lines 17-21).

Regarding Claim 3, Caskey et al teach the method using multiple detector primers, each comprising different diagnostic nucleotides (e.g. M vs S or Z, Example 4).

Regarding Claim 4, Caskey et al teach the method wherein the two primers are used to identify which of two possible SNP is present (e.g. M vs S or Z, Example 4).

Regarding Claim 5, Caskey et al teach the method wherein four detector primers are used (e.g. M (1) vs Z (2) and M(3) vs S(4), Example 4).

Regarding Claim 7, Caskey et al teach the method wherein detector primers have a non-diagnostic mismatch (Column 5, lines 20-46).

Regarding Claim 8, Caskey et al teach the method wherein the non-diagnostic nucleotide is within 15 nucleotides of the detector nucleotide i.e. the primers are preferably 12-16 (Column 4, lines 39-40). Hence, the non-diagnostic nucleotide is within 15 as claimed.

Regarding Claim 11, Caskey et al teach the method wherein the detector primer is 15-36 nucleotides (Column 4, lines 37-41).

Regarding Claim 12, Caskey et al teach the method wherein the detector primer is 18-24 nucleotides (Column 4, lines 37-41).

Regarding Claim 13, Caskey et al teach the method wherein the amplification is nucleic acid based amplification (Column 7, lines 31-50).

Regarding Claim 14, Caskey et al teach the method wherein the detector primer is 12-50 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 15, Caskey et al teach the method wherein the detector primer is 12-24 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 16, Caskey et al teach the method wherein the detector primer is 12-19 nucleotides (Column 4, lines 37-41 and Examples 3-4).

Regarding Claim 17, Caskey et al teach the method wherein the SNP is detected by means of a label attached to the primer (Column 6, lines 16-35).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 6 and 18-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996) in view of Whitcombe et al (U.S. Patent No. 6,326,145, filed 25 November 1998).

Regarding Claims 6 and 18-22, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the

target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. β^+ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54).

Caskey et al also teach primers labeled using art recognized techniques (Column 6, lines 16-35) but they do not teach tailed primers, primers detectable upon extension, primers labeled with donor/quencher dyes, quantitatively detected and displaced by an upstream primer.

However, these elements were well known in the art at the time the claimed invention was made as taught by Whitcombe et al (Column 4, lines 31-65) wherein binding results in abolished signal (Column 4, lines 49-53). Whitcombe et al further teach their method is useful for strand displacement (Column 5, lines 57-59) and especially quantitative allele discrimination (Column 6, lines 33-43 and Column 10, line 60-Column 11, line 17).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the tailed primers having donor/quencher dye attached as taught by Whitcombe et al to the allele-specific primers of Caskey et al for the expected benefit of providing quantitative analysis of clinically important nucleic acids e.g. HIV nucleic acids as taught by Whitcombe et al (Column 6, lines 33-43).

9. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Caskey et al (U.S. Patent No. 5,578,458, issued 26 November 1996).

Regarding Claims 9-10, Caskey et al disclose a method for identifying a single nucleotide polymorphism (SNP) in an isothermal reaction (e.g. extension with DNA polymerase (Klenow) Column 8, lines 7-30). Caskey et al teach the method comprising hybridizing to the target a detector primer having a diagnostic nucleotide "about" 4 nucleotides 5' of the 3' terminal nucleotide (i.e. n-5 is deemed about 4), amplifying the target, determining the efficiency of extension relative to a non-diagnostic primer and detecting the SNP based on efficiency of extension (e.g. $\beta+$ vs β^s, Example 3 and M vs S or Z, Example 4 and Column 5, lines 46-54).

Caskey et al further teach detector primers having non-diagnostic mismatch nucleotides whereby the more perfectly matched primer will be favored in the amplification reaction (Column 5, lines 20-46). Caskey et al also teach the primers are preferably 12-16 (Column 4, lines 39-40) and they illustrate diagnostic nucleotides positioned 5 bases from the terminal nucleotide (Examples 3-4). They do not specifically teach the non-diagnostic nucleotide 5 nucleotides from or adjacent to the diagnostic nucleotide. However, the addition of a non-diagnostic nucleotide (as they clearly suggest) to their exemplified 12 nucleotide primers would position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide. Hence, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add a non-diagnostic nucleotide to the diagnostic primer of Caskey and to position the non-diagnostic nucleotide adjacent to or within 5 nucleotides of the diagnostic nucleotide based on the available nucleotide positions within the 12 nucleotide primers exemplified by Caskey et al.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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Art Unit: 1634
August 19, 2004